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EXAMINER	
HENLEY III, RAYMOND J	

ART UNIT	PAPER NUMBER
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/614,233	EBDRUP ET AL.	
	Examiner	Art Unit	
	Ray Henley	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-35* is/are rejected.

7)☒ Claim(s) *7,8,16 and 23-26* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/5/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

CLAIMS 1-35 ARE PRESENTED FOR EXAMINATION

Applicants' Information Disclosure Statement filed September 5, 2003 has been received and entered into the application. As reflected by the attached, completed copy of form PTO-1449 (1 page), the cited references have been considered.

Claim Objections

Claims 7, 8, 16 and 23-26 are objected to because of the following informalities:

Claims 7 and 8 depend from claims directed to methods and thus, at line 1 of each, the term "use" should be changed to ---method---.

In claim 16, penultimate line, there should be a space between "and" and "5,5-Dimethyl..".

In claims 23 and 24, "a boronic acid, an ester thereof, a prodrug thereof" should read as ---said boronic acid, said ester thereof, said prodrug thereof--- because these claims depend from claims where "a boronic acid, an ester thereof, a prodrug thereof" is set forth and thus should refer to these specific compounds.

In claims 25 and 26, line 1 of each, "pharmaceutical composition" should be changed to ---method--- because these claims depend from claims directed a method. Also, further appropriate amendments should be made to provide for proper further limitations of the composition set forth in the claims from which claims 25 and 26 depend, i.e., "The method of claim...wherein said pharmaceutical composition..."

Appropriate correction is required.

Claim Rejection - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 31-35 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating insulin resistance, diabetes type 1, diabetes type 2, metabolic syndrome X, impaired glucose tolerance, hyperglycemia, dyslipidemia, hyperlipoproteinemia, hypertriglyceridemia, hyperlipidemia, hypercholesterolemia, or other abnormalities of lipoprotein metabolism in patient in need thereof, does not reasonably provide enablement for a method of treating, in general, a patient who suffers from the above mentioned diseases/disorders.

The diseases/disorders set forth in claim 31 modify the intended host rather than the therapeutic objective of "treating". The claims read on administering the claim defined boronic acid compounds for any therapeutic purpose in the patient population defined in the claim. Such reads on a panacea however and the art currently is unaware of any single agent, or combination of agents that could be used for the treatment of any and all disease states which is encompassed by the present claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

When the above factors as applied to the present application (see below) are weighed, it is the examiner's position that the present specification would only enable the

skilled artisan to practice a method of treatment wherein the therapeutic objective of such treatment has been set forth.

(1) The nature of the invention.

The claim 31 sets forth a method of treating a host who is defined by the disorder he/she is suffering. The claim is silent as to the therapeutic objective to be achieved by such treating.

(2) The state of the prior art.

The art currently is unaware of any single agent, or combination of agents that could be used for the treatment of any and all disease states which is encompassed by the present claims.

(3) The relative skill of those in the art.

The relative skill of those in the art is high.

(4) The predictability or unpredictability of the art.

In the pharmaceutical art, there is a reasonable degree of predictability. For example, where it is known that a particular drug with a particular mechanism of action is effective for treating a specific type of disease/disorder, it can be reasonably predicted that another drug, whether structurally similar or not, that possess the same mechanism of action would also be useful for treating the same specific type of disease or disorder. Here, however, the art is unaware of any single drug, or combination of drugs, that could be used for the treatment of any unspecified disease or all diseases in general.

(5) The breadth of the claims.

The claims set forth merely a method of treating a host who is defined by the disorder he/she is suffering. The therapeutic objective to be achieved by such treatment is not set forth.

(6) The amount of direction or guidance presented.

There is adequate direction and guidance provided throughout the present specification that would enable the skilled artisan to practice a method of treating insulin resistance, diabetes type 1, diabetes type 2, metabolic syndrome X, impaired glucose tolerance, hyperglycemia, dyslipidemia, hyperlipoproteinemia, hypertriglyceridemia, hyperlipidemia, hypercholesterolemia, or other abnormalities of lipoprotein metabolism through the administration of the disclosed boronic acid compounds. This, however, is not commensurate in scope with the claimed invention as it is directed to the broad objective of "treating a patient" who may suffer from any one of various diseases/disorders.

(7) The presence or absence of working examples.

The present specification contains no working examples that would enable the skilled artisan to practice the invention of the scope presently claimed.

(8) The quantity of experimentation necessary.

Because of the fact that the art is currently unaware of a drug that is broadly useful for "treating a patient", no amount of experimentation, undue or otherwise, could be employed by the skilled artisan to arrive at the claimed objective.

In order to overcome the present rejection, applicants may wish to consider amending claim 31 to recite:

"31. A method for treating insulin resistance, diabetes type 1, diabetes type 2, metabolic syndrome X, impaired glucose tolerance, hyperglycemia, dyslipidemia, hyperlipoproteinemia, hypertriglyceridemia, hyperlipidemia, hypercholesterolemia, or other abnormalities of lipoprotein metabolism, said method comprising administering to a patient in need thereof...".

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-30 and 32-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claim 1 (line 6) [and thus its dependents], the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim 17 is not clear as to the manner in which it further limits the previous claim. It is believed that if it were amended to recite, in part, "wherein the compound is R^3-$B(OH)_2$ and the pK_a of the R^3 substituent is...".

Claims 2, 10, 17, 19-21, 25 and 32 contain a broad range together with a narrow range that falls within the broad range, e.g., in claim 2 a broad range of pK_a values of between 2.0 and 11.5 is set forth and is then followed by several other ranges which are narrower in scope.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the

decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

I Claims 1, 2, 6, 9, 10, 14, 15, 17-32 are rejected under 35 U.S.C. 102(a) as being anticipated by Holmes-Farley et al. (U.S. Patent Application Publication No. 2003/0064963) who teach methods of treating obesity, Type II diabetes mellitus, impaired glucose tolerance, lipid syndromes, hyperglycemia, hypertriglyceridemia, and hyperlipidemia (page 4, cols. 1-2, section [0046] which comprises administering from about 5 mg/day to about 10 grams/day (page 4, col. 2, section [0048] by a route that may be oral, rectal, nasal, pulmonary or topical (page 4, col. 1, section [0045] of a pharmaceutical composition which may comprise an acceptable pharmaceutical carrier (page 4, col. 2, section [0047] and boronic acid compounds, including esters and salts, encompassed by the present claims (see the first row of chemical compounds depicted in Figure 4A, 4D, 4E; col. 1, sections [0005] – [0010]; page 2, col. 1, section [0022]; page 2, col. 2, section [0027]; page 4, col. 1, section [0043]; and page 4, col. 2, section [0050]) Compare the structures of Holmes-Farley et al. with the definition provided in present claim 6 and in claim 9 there the R^3 substituent may be a phenyl substituted with a C1-6 alkyl which in turn my be substituted with an oxo and a halo group.

The biochemical processes and physical constants of present claims 1, 2, 10, 18-21 and 32 are deemed to be inherent properties of the prior art compounds because the same compounds are administered to the same patient populations in both the prior art and the present claims and the prior art compounds are within the scope of the present claims.

II Claims 1, 2, 18, 19 and 21-32 are rejected under 35 U.S.C. 102(a) as being anticipated by Henderson et al. (U.S. Patent Application Publication No. 2002/012832) who teaches the treatment of diabetic retinopathy (page 1, col. 2, section [0008]) which comprises administering from between about 0.001 to 500 mg (page 8, col. 2, section [0144] by a route that may be oral, rectal, percutaneous or parenteral (page 7, col. 2, section [0139] of a pharmaceutical composition which may comprise an acceptable pharmaceutical carrier (page 7, col. 2, section [0139] and boronic acid compounds, including salts thereof (page 2, col. 2, section [0031] and page 6, col. 2, section [0106].

The patients of the prior art suffer from diabetic retinopathy and therefore diabetes and thus are the patient population of the present claims. The biochemical processes of claim 1 are deemed to be inherent in the prior art compound because such compound is administered to the same host. Also, because of the close structural similarity between the prior art compound and those of the present invention where R^3 may be a substituted heteroaryl moiety (see present claim 6, for example), it is believed that that the physical constants as in present claims 2, 10, 18, 19, 21 and 32 would also be inherent.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

I Claims 22, 25, 26 and 33-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Holmes-Farley et al., as above.

The differences between the above and the claimed subject matter lie in that Holmes-Farley et al. fail to teach:

(1) a parenteral route of administration; and

(2) the presently claimed duration of treatment and dosage range.

However, to the skilled artisan, the claimed subject matter would have been obvious because:

(1) The reference teaches various routes of administration and thus the skilled artisan would have appreciated that the drugs could be introduced into the body through

various routes. The artisan would have been motivated to employ a parenteral route of administration because it is an easy means of administration and was one that was well known to the skilled artisan. Also, the artisan would have also taken into consideration the patient's acceptance of any given route of administration; and

(2) The dosages taught by the reference are characterized as being only "typical" (page 4, col. 2, section [0048], line 6). The skilled artisan would have been motivated to vary the dosages, as well as the duration of treatment based upon the patient's individual characteristics such as general health, severity of disease, age, sex, body weight and tolerance to drugs.

II Claims 22, 25, 26 and 33-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Henderson, as above.

The differences between the above and the claimed subject matter lie in that Holmes-Farley et al. fail to teach:

(1) a nasal or pulmonary route of administration; and

(2) the presently claimed duration of treatment and dosage range.

However, to the skilled artisan, the claimed subject matter would have been obvious because:

(1) The reference teaches various routes of administration and thus the skilled artisan would have appreciated that the drugs could be introduced into the body through various routes. The artisan would have been motivated to employ any of the known routes of administration in order to ensure proper compliance with the prescribed therapy and would have also taken into consideration the patient's acceptance of any given route of administration; and

(2) The dosages taught by the reference are characterized as being only "general" (page 8, col. 2, section [0144], line 1). The skilled artisan would have been motivated to vary the dosages, as well as the duration of treatment, based upon the patient's individual characteristics such as general health, severity of the disease, age, sex, body weight and tolerance to drugs.

Accordingly, for the above reasons, the claims are deemed properly rejected/objected to and none are allowed.

The Spielvogel et al. reference (U.S. Patent 5,312,816) is relevant to the presently claimed subject matter and has been cited by the Examiner merely to the general state of the art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ray Henley whose telephone number is 571-272-0575. The examiner can normally be reached on M-F, 8:30 am to 4:00 pm Eastern Time.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel can be reached on 571-272-0584. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ray Henley
Primary Examiner
Art Unit 1614

Mar. 24, 2004